

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
28 February 2002 (28.02.2002)

PCT

(10) International Publication Number
WO 02/15698 A1

(51) International Patent Classification⁷: A01N 59/16. (25/10)

(81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.

(21) International Application Number: PCT/GB01/03686

(22) International Filing Date: 17 August 2001 (17.08.2001)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
0020628.4 22 August 2000 (22.08.2000) GB
0021119.3 29 August 2000 (29.08.2000) GB

(84) Designated States (regional): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CI, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

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Published:

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— with international search report

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

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WO 02/15698 A1

(54) Title: PREPARATION OF ARTICLES HAVING A CONTACT BIOCIDAL PROPERTY

(57) Abstract: In a process for the preparation of an article a contact biocidal property, there is provided a polymer solution which contains atomic/metallic silver in suspension or complexed with the polymer and/or which contains a silver compound in solution, in suspension or complexed with the polymer. This polymer solution is applied to a substrate by impregnation or surface deposition, thus coating the substrate. Alternatively, it is possible to convert the polymer solution to a fibre, film, powder or foam, effectively forming the article from the polymer solution instead of coating an existing article. In either case, any silver compound present is reduced to atomic/metallic silver, and the resultant article is dried. Chitosan is preferably used as the polymer, although poly(vinyl alcohol) and sodium alginate can also be used. The polymer may be cross-linked at a suitable point in the process to insolubilize it.

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TITLE

Preparation of Articles having a Contact Biocidal Property

5 DESCRIPTION

This invention relates to the preparation of articles having a contact biocidal property derived from atomic or metallic silver dispersed uniformly through the articles or through a surface coating on the articles. The articles having the contact biocidal 10 property have a wide range of applications, especially in the health care and associated industries. Articles prepared according to the invention have a characteristic that effectively kills a wide range of micro-organisms which come in contact with the articles.

15 It is known that atomic/metallic silver is a highly effective contact biocide. US 5817325 and US 5849311 give examples of the application of an organic coating to a substrate followed by immersion of the coated substrate in a bath containing a silver salt. US 4960413 describes the production of a wound dressing by immersion of chitosan-containing fungal fibres, or non-woven material prepared from them, in 20 silver nitrate solution.

The invention provides a process for the preparation of an article having a contact biocidal property, the process comprising the steps of

(a) providing a polymer solution which contains atomic/metallic silver in suspension 25 or complexed with the polymer and/or which contains a silver compound in solution, in suspension or complexed with the polymer,

(b) either applying the polymer solution to a substrate by impregnation or surface deposition or converting the polymer solution to a fibre, film, powder or foam,

(c) reducing the silver compound, if present, to atomic/metallic silver, and 30

(d) drying the resultant article.

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Polymers suitable for use in the invention include water-soluble and organo-soluble polymers. The preferred water-soluble polymer is chitosan, which is known to exhibit the property of attracting and inactivating a wide range of micro-organisms. Other suitable water-soluble polymers are poly(vinyl alcohol) and sodium alginate or other soluble salts of alginic acid.

It is preferred that the polymer solution provided in step (a) contains atomic/metallic silver. Such a polymer solution may be prepared by reducing an aqueous solution or suspension of a silver compound to atomic/metallic silver by chemical or photochemical means and subsequently dissolving the polymer in the resultant suspension. An alternative preparation comprises admixing an aqueous solution of the polymer with an aqueous solution or suspension of a silver compound and subsequently reducing the silver compound to atomic/metallic silver by chemical or photochemical means. If the polymer used is chitosan, the polymer solution may be prepared by slurring chitosan with a soluble silver salt to prepare a chitosan/ Ag^+ complex, dissolving the chitosan/ Ag^+ complex in a suitable aqueous acid and photochemically reducing the silver ions in the chitosan/ Ag^+ solution to atomic/metallic silver. The photochemical reduction may be effected earlier in the process, which then comprises slurring chitosan with a soluble silver salt to prepare a chitosan/ Ag^+ complex, photochemically reducing the silver ions in the chitosan/ Ag^+ complex to atomic/metallic silver, and dissolving the chitosan/ Ag° complex in a suitable aqueous acid.

The polymer solution provided in step (a) may, however, contain a silver compound in solution, in suspension or complexed with the polymer. In this case it is necessary to perform step (c) after step (b) of the process.

Although chemical reduction is possible, photochemical reduction is preferred for reasons of practicality. In this case it is advantageous to convert any soluble silver salt, for example silver nitrate or silver perchlorate, to one of the relatively insoluble

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and highly photosensitive silver halides (chloride, bromide or iodide, or mixtures of these) before exposure to ultraviolet/visible light.

Depending on the intended end use, it may be desirable to insolubilise the polymer
5 after step (b) by crosslinking or other means. This may be effected immediately after
step (b), after step (c) if that step is performed, or during or after step (d).

In step (b) of the process of the invention, the polymer solution is *either* applied to a
substrate by impregnation or surface deposition *or* converted to a fibre, film, powder
10 or foam. Application to a substrate, particularly a fibrous substrate, is preferred. The
fibres may be organic, inorganic or metallic fibres or blends of these. The fibres of the
substrate may be loose fibres or form sliver, rove, yarn, woven or knitted fabric, non-
woven material including paper products, or garments made from any of these.
Preferred fibres include cotton or other cellulose-based natural or man-made fibres
15 (e.g. viscose rayon), wool or other protein-based fibres, and polyamide, polyester,
polyolefin (e.g. polypropylene), polysaccharide and carbon fibres. Other usable fibres
include those made from alginic acid and its salts, polyacrylic acid and its salts,
poly(methacrylic acid) and its salts, or carboxymethyl cellulose and its salts or
mixtures thereof either with each other or with the fibres previously mentioned. The
20 fibrous substrate may be given additional chemical or physical treatment(s) prior to or
subsequent to the application of the silver/polymer coating. The substrate may
alternatively be a film, foam or membrane or an article formed from a film, foam or
membrane. The film, foam or membrane may, for example, be composed of cellulose,
polyamide, polyester, poly(tetrafluoroethylene) or a related polymer in which one or
25 more of the fluorine atoms in the monomer has (have) been replaced by chlorine
atom(s), polyacrylic, polypropylene, alginic acid or its salts, polyacrylic acid or its
salts, poly(methacrylic acid) or its salts, carboxymethyl cellulose or its salts, or
carragheenan. Deposition of the polymer solution on the substrate may be carried out
by padding, printing, spraying or pressure impregnation. An alternative to application
30 of the polymer solution to a substrate is to convert the polymer solution into fibre,
film, foam or powder by the techniques normally used for these conversions,

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effectively forming the article from the polymer solution instead of coating an existing article. In this case the atomic/metallic silver will be present throughout the article rather than concentrated in a surface layer.

5 The process according to the invention effectively disperses atomic/metallic silver through the article or through a surface coating on the article in such a way that the silver substantially or wholly retains its biocidal properties. The concentration of silver in the polymer solution can be adjusted accurately to the required value before deposition on the substrate (or conversion of the polymer solution into fibre, film,
10 foam or powder), so ensuring a precise and reproducible level of treatment with the minimum waste of expensive silver compounds. This accurate control of the silver concentration is not possible with methods involving immersion of the article in a bath containing a silver compound. The inclusion of the silver in the polymer solution before application to the substrate (or conversion of the polymer solution into fibre,
15 film, foam or powder) is an essential feature of the invention and reduces the number of stages in the process.

For most applications it is desirable to have the silver present wholly (or as nearly so as is practicable) as atomic/metallic silver. In this form it is insoluble and will not be
20 leached out, so that the article will retain its biocidal properties. However for some applications it may be desirable to have a proportion of the silver present either as a soluble salt or as a relatively insoluble salt with a finite, but very limited, aqueous solubility. The precise nature and composition of the silver in the coating will depend on the ionic species present in, or introduced into, the reaction process, the pH, and
25 the extent of reduction.

The invention is illustrated by the following Examples.

Example 1

30 A 2% solution of chitosan [DA = 0.16] in 0.2 M lactic acid was prepared and 100 ml of this solution mixed with 0.68 g AgNO₃ dissolved in 50 ml 0.1 M lactic acid. A

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sample of cotton fabric was padded with this to give ~ 110% pick-up, then oven-dried at 45°C. The fabric gradually developed a grey colour on exposure to light, indicating that photochemical reduction was taking place.

5 Example 2

A 2% solution of chitosan [DA = 0.16] in 0.2 M lactic acid was prepared and 100 ml of this solution mixed with 0.68 g AgNO₃ dissolved in 50 ml 0.1 M lactic acid. A solution of 0.25 g NaCl in 10 ml distilled water was run in slowly with stirring to give a white opaque suspension of AgCl in chitosan. This was padded on to a sample
10 of polyester/cotton blend fabric, the sample dried at 45°C, then neutralised in 2% NH₄OH solution, rinsed and developed photochemically by UV irradiation.

Example 3

Chitosan [DA = 0.16] (11 g) was dissolved in 900 ml 0.1 M acetic acid and filtered to
15 remove insoluble material. The filtered solution was stirred while a solution of 4.25 g AgNO₃ in distilled water was added. Once mixed, a solution of 1.61 g NaCl in 100 ml 0.1 M acetic acid was added to give a rapid precipitation of finely dispersed AgCl which gradually changed from white to a purplish grey, indicating photochemical conversion of the silver species present from Ag⁺ to Ag⁰. This was then developed by
20 irradiating with uv/visible light, while stirring, to further reduce the Ag⁺ photochemically.

Three samples of cotton fabric were padded with this solution to approximately 100% pickup, dried, then reduction was completed chemically by (a) steeping in a bath
25 containing hydroquinone/sodium hydroxide/sodium metabisulphite, rinsing and drying; (b) treating at 90°C in a bath containing D-glucose/sodium hydroxide, rinsing and drying; (c) treating at 90°C in a bath containing D-glucose/sodium carbonate, rinsing and drying.

30 The three samples, together with a control sample of cotton fabric padded with chitosan containing no silver, were tested for antibacterial activity against methicillin-

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resistant *Staphylococcus aurus* NCTC 4163 using the SNV 195 924 method. All three silver-containing samples showed Grade 1 antibacterial activity, a 100% kill with a 2 mm zone of inhibition. The control sample showed only Grade 4 (partial) antibacterial kill.

5

Example 4

Chitosan [DA = 0.16] (2.5 g) was dissolved in 900 ml 0.1 M acetic acid and filtered to remove insoluble material. The filtered solution was stirred while a solution of 4.0 g AgNO₃ in 25 ml distilled water added slowly, care being taken to ensure that it is well mixed during the addition. Then a solution of 1.38 g NaCl in 25 ml distilled water was added and the mixture stirred in the presence of light to bring about photochemical conversion of the silver species present from Ag⁺ to Ag⁰. A 300 ml portion of the suspension was taken and stirred while an additional 2.25 g of chitosan, dampened with methanol to aid its dispersion, was added, followed by 0.75 ml glacial acetic acid. A sample of cotton was padded with this solution to approximately 110% uptake, dried and sent for testing for antibacterial activity against methicillin-resistant *Staphylococcus aurus* NCTC 4163 using the SNV 195 920 qualitative plate test and the quantitative SNV 195 924 test. The sample showed Grade 1 antibacterial activity "with good effect and with pronounced inhibition zone", in the first test, and very impressive and highly significant antibacterial activity in the second test.

Example 5

A 100 ml portion of a chitosan/silver mixture containing 0.5 g chitosan and 0.4 g "silver" in 0.1 M acetic acid was produced as described in Example 3 and mixed with 100 ml of a 0.5 % chitosan solution, also in 0.1 M acetic acid. A sample of cotton was padded with this solution to approximately 110% uptake, dried, and sent for testing for antibacterial activity against methicillin-resistant *Staphylococcus aurus* NCTC 4163 using the SNV 195 920 qualitative plate test and the quantitative SNV 195 924 test. The sample showed Grade 1 antibacterial activity "with good effect and with

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pronounced inhibition zone", in the first test, and very impressive and highly significant antibacterial activity in the second test.

Example 6

5 A solution containing 4 g poly(vinyl alcohol) and 0.8 g AgNO₃ in 200 ml distilled water was prepared and stirred while 0.275 g NaCl in 10 ml distilled water was added. The suspension was stirred in daylight to promote the photochemical conversion of the silver species present from Ag⁺ to Ag⁰. A solution of potassium dichromate (0.3 g) in 10 ml distilled water was added and the mixture used to pad a sample of
10 cotton/polyester fabric to about 120% pickup. The padded fabric was dried, exposed to UV irradiation to bring about cross-linking, then sent for testing for antibacterial activity against methicillin-resistant *Staphylococcus aureus* NCTC 4163 using the SNV 195 920 qualitative plate test and the quantitative SNV 195 924 test. The sample showed Grade 1 antibacterial activity "with good effect and with pronounced
15 inhibition zone", in the first test, and particularly impressive and highly significant antibacterial activity in the second test.

Example 7

A sample of chitosan (2 g) was dissolved in 400 ml 0.1 M acetic acid, filtered and
20 stirred while a solution of 0.8 g AgNO₃ in 10 ml distilled water was added. Stirring was continued while the mixture was being irradiated with uv/visible light until it was converted to a purplish-grey colour. A portion of this mixture was diluted to twice the volume then padded onto a sample of activated carbon fibre to give 145% uptake. The sample was oven-dried at 50°C, neutralised in dilute ammonia, rinsed well and oven-dried again. This was sent for testing for antibacterial activity against methicillin-resistant *Staphylococcus aureus* NCTC 4163 using the SNV 195 920 qualitative plate test. The test showed that there was no zone of inhibition, i.e. no diffusion of any antibacterial ingredient from the coating into the culture medium, but zero growth underneath, i.e. 100% kill of all bacteria on contact.
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Example 8

A portion of the undiluted chitosan/silver solution prepared in Example 7 was placed in an ASL 500 home spray container and sprayed onto a sample of cotton fabric to effect treatment on one side of the fabric only.

5

Example 9

A solution of AgNO_3 (1.8 g) in 400 ml distilled water was stirred while NaCl (0.62 g) in 10 ml distilled water was added dropwise. Sodium alginate (4 g) was added to the suspension and stirring continued with irradiation with uv/visible light to bring about
10 photochemical conversion of Ag^+ to Ag° . The solution was then padded onto a cotton fabric to give approximately 110% pick-up, then oven dried. A second sample, treated in the same way, was given a final treatment by steeping in a 2% CaCl_2 solution, then rinsed and dried.

15 Example 10

Chitosan (8 g) was dissolved in 400 ml 0.2 M acetic acid, filtered to remove any insoluble particles, and stirred while a solution of 0.8 g AgNO_3 in 10 ml distilled water was added. Stirring was continued while the mixture was being irradiated with uv/visible light until it was converted to a purplish-grey colour. A further 32 g
20 chitosan flake was added, mixed well in, then 10 ml glacial acetic acid added while the thickening solution was stirred. The viscous mass was let stand for 24 hours, then used to print on a range of fabrics: a) a 100% cotton fabric; b) a 70:30 cotton:polyester blend fabric; c) an activated carbon fibre fabric; d) a 100% alginate fibre fabric; e) a 80:20 alginate:viscose blend fabric.

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CLAIMS

1. A process for the preparation of an article having a contact biocidal property, the process comprising the steps of
 - 5 (a) providing a polymer solution which contains atomic/metallic silver in suspension or complexed with the polymer and/or which contains a silver compound in solution, in suspension or complexed with the polymer,
 - (b) either applying the polymer solution to a substrate by impregnation or surface deposition or converting the polymer solution to a fibre, film, powder or
10 foam,
 - (c) reducing the silver compound, if present, to atomic/metallic silver, and
 - (d) drying the resultant article.
2. A process according to claim 1 wherein the polymer is a water-soluble polymer or
15 water-soluble polymer derivative.
3. A process according to claim 2 wherein the polymer is chitosan.
4. A process according to claim 2 wherein the polymer is poly(vinyl alcohol).
20
5. A process according to claim 2 wherein the polymer is sodium alginate or any other water soluble salt of alginic acid.
6. A process according to claim 1 wherein the dissolved polymer is an organo-soluble polymer or organo-soluble polymer derivative.
25
7. A process according to any of claims 1 to 5 wherein the polymer solution contains atomic/metallic silver in suspension and is prepared by reducing an aqueous solution or suspension of a silver compound to atomic/metallic silver by chemical or photochemical means and subsequently dissolving the polymer in the resultant suspension.
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8. A process according to any of claims 1 to 5 wherein the polymer solution contains atomic/metallic silver in suspension and is prepared by admixing an aqueous solution of the polymer with an aqueous solution or suspension of a silver compound and subsequently reducing the silver compound to atomic/metallic silver by chemical or photochemical means.
5
9. A process according to claim 3 wherein the polymer solution contains atomic/metallic silver complexed with the chitosan and is prepared by slurring chitosan with a soluble silver salt to prepare a chitosan/ Ag^+ complex, dissolving the chitosan/ Ag^+ complex in a suitable aqueous acid and photochemically reducing the silver ions in the chitosan/ Ag^+ solution to atomic/metallic silver.
10
10. A process according to claim 3 wherein the polymer solution contains atomic/metallic silver complexed with the chitosan and is prepared by slurring chitosan with a soluble silver salt to prepare a chitosan/ Ag^+ complex, photochemically reducing the silver ions in the chitosan/ Ag^+ complex to atomic/metallic silver, and dissolving the chitosan/ Ag^o complex in a suitable aqueous acid.
15
11. A process according to any of claims 1 to 6 wherein the polymer solution used in step (b) contains a silver compound and step (c) is performed by chemical or photochemical means.
20
12. A process according to any preceding claim further comprising crosslinking the polymer after step (b).
25
13. A process according to claim 11 further comprising crosslinking the polymer after step (c).
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14. A process according to any of claims 1 to 11 further comprising crosslinking the polymer during step (d).
15. A process according to any of claims 1 to 11 further comprising crosslinking the polymer after step (d).
16. A process according to any preceding claim wherein the polymer solution is applied to a substrate comprised of organic, inorganic or metallic fibres or blends of such fibres.

10

17. A process according to claim 16 in which the fibres of the substrate are loose fibres or form sliver, rove, yarn, woven or knitted fabric, non-woven material including paper products, or garments made from any of these.
- 15 18. A process according to claim 16 or claim 17 wherein the fibres are cotton or other cellulose-based natural or man-made fibres, wool or other protein-based fibres, or polyamide, polyester, polyacrylic, polyolefin, polysaccharide or carbon fibres, or mixtures thereof.
- 20 19. A process according to claim 16 or claim 17 wherein the fibres are made from alginic acid and its salts, polyacrylic acid and its salts, poly(methacrylic acid) and its salts, or carboxymethyl cellulose and its salts or mixtures thereof either with each other or with the fibres listed in claim 18.
- 25 20. A process according to any of claims 1 to 15 wherein the polymer solution is applied to a substrate which is a film, foam or membrane or an article formed from a film, foam or membrane.
- 30 21. A process according to claim 21 wherein the film, foam or membrane is composed of cellulose, polyamide, polyester, poly(tetrafluoroethylene) or a related polymer in which one or more of the fluorine atoms in the monomer has (have) been

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replaced by chlorine atom(s), polyacrylic, polypropylene, alginic acid or its salts, polyacrylic acid or its salts, poly(methacrylic acid) or its salts, carboxymethyl cellulose or its salts, or carragheenan.

INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 01/03686

A. CLASSIFICATION OF SUBJECT MATTER
 IPC 7 A01N59/16 // (A01N59/16, 25:10)

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
 IPC 7 A01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P, X	WO 00 49219 A (FOXWOOD RES LTD (GB)) 24 August 2000 (2000-08-24) the whole document	1-21
X	PATENT ABSTRACTS OF JAPAN vol. 016, no. 144 (C-0927), 10 April 1992 (1992-04-10) & JP 04 002877 A (NICHIBI:KK), 7 January 1992 (1992-01-07) abstract	1-21
X	PATENT ABSTRACTS OF JAPAN vol. 015, no. 181 (C-0830), 9 May 1991 (1991-05-09) & JP 03 045709 A (NICHIBI:KK), 27 February 1991 (1991-02-27) abstract	1-21
		-/-

 Further documents are listed in the continuation of box C. Patent family members are listed in annex.

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Date of the actual completion of the international search

28 November 2001

Date of mailing of the international search report

04/12/2001

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INTERNATIONAL SEARCH REPORT

Int'l Application No
PCT/GB 01/03686

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 4 960 413 A (SAGAR BRIAN ET AL) 2 October 1990 (1990-10-02) the whole document	

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/GB 01/03686

Patent document cited in search report		Publication date		Patent family member(s)		Publication date
WO 0049219	A	24-08-2000	AU EP WO	2565400 A 1157158 A1 0049219 A1	04-09-2000 28-11-2001 24-08-2000	
JP 04002877	A	07-01-1992	NONE			
JP 03045709	A	27-02-1991	NONE			
US 4960413	A	02-10-1990	EP EP GB	0291587 A1 0460774 A2 2182560 A ,B	23-11-1988 11-12-1991 20-05-1987	